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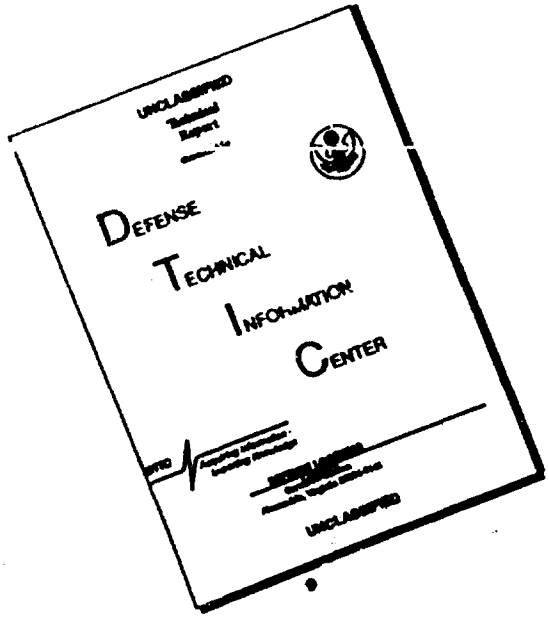

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EXPERIENCE IN THE TREATMENT OF STAPHYLOCOCCAL DISEASES IN INFANTS BY USING STAPHYLOCOCCAL ANATOXIN

[Following is the translation of an article by L. A. Rudneva, Lvov Scientific-Research Institute for Maternity and Childhood Protection (Director-Master of Medical Sciences L. Ya. Davydov), published in the Russian-language periodical Pediatriya (Pediatrics), 43:8-13, October 1964, It was submitted on 7 April 1964. Translation performed by Sp/7 Charles T. Ostertag, Jr.]

In recent years in our country and abroad a steady increase has been observed in the specific importance of staphylococcal diseases in the pathology of children in the first year of life (Yu. F. Dombrovskaya; P. A. Ponomareva; A. R. Shurinok; I. A. Shtern). Children come down with staphylococcal infections most often during the first 3 months of life (Ye. I. Semonova).

The increase in the resistance of staphylococci to antibiotics and sulfanilamides has created great difficulties in the treatment of staphylococcal diseases, and frequently complex therapy turns out to be ineffective. Besides this, antibiotics depress the immunological reactivity of an organism (human subject) (Kh. Kh. Planelyes and N. V. Chumachenko; N. I. Pokoziy; Yu. M. Mikhaylova), which also has an unfavorable influence on the results of treatment. Therefore, in the therapy of severe forms of staphylococcal infections [they] clinicians are resorting to the use of staphylococcal toxoid for the purpose of stimulating the specific immunological reactivity of the infant.

At the present time staphylococcal toxoid is being used for the treatment of staphylococcal diseases in children. A. R. Shurinok, Ye. K. Yatsimirskaya and R. D. Nikolayev, and V. I. Nosovskaya observed a favorable influence on the recovery process following the administration of staphylococcal toxoid to sick children.

One of the additional and reliable criteria of a positive influence of toxoid is the increase in the titer of staphylococcal antitoxin. In healthy babies the level of staphylococcal antitoxin in the blood, based on data from the literature, fluctuates from 0.25 to 2 AU.

The content of staphylococcal antitoxin in the blood of young children during staphylococcal infections and during treatment of this age group has not been studied sufficiently.

The purpose of this work was the study of the effectiveness of staphylococcal toxoid for the treatment of babied with staphylococcal diseases.

A total of 89 patients were observed. Of these, 47 received staphylococcal toxoid in the complex of medicines. The remaining 42 served as a control.

Prior to admission into the clinic the children were located in district and regional hospitals where they received 1-2 and more antibacterial preparations without noticeable success.

The patients were hospitalized in various periods from the onset of illness: During the 1st week 16 children were admitted, in 2-4 weeks - 15, in 2-3 months - 16. In the control group 18 children were admitted in the 1st week of illness, 11, in the 2-4th week, and 13 in the 2-3rd month. Thus, there were no significant differences in the periods of hospitalization of the patients of both groups.

The clinical characteristics of the sick children are presented in Table 1.

Based on the indices presented in Table 1, both groups of children were basically the same.

Based on the nature of the disease and the severity of the course both groups of children were also equivalent (Table 2).

The treatment of the patients was complex (hygienic-dietetic regulation, vitamins, blood infusion, plasma, antibiotics, etc.). Along with the generally accepted therapy 47 of the children received native staphylococcal toxoid. The latter was injected together with Novocaine subcutaneously into the subscapular area. Different doses of toxoid were used. Thus, 20 children received the toxoid in increasing doses in accordance with the instructions of the N. F. Gamaleya Institute of Epidemiology and Microbiology. The sequence of administration was 0.1 - 0.3 - 0.5 - 0.7 - 1.0 - 1.2 - 1.5 - 1.7 - 2.0 ml with intervals of 3-5 days between injections. When using such a method of administration, especially with the injection of large doses (1 ml and more), we observed in the children a reddening of the skin and a small induration at the site of administration of the toxoid. This lasted for 2-4 days. A noticeable general reaction was not observed.

The other group of children (27) received the toxoid in smaller amounts, the maximum dose did not exceed 1 ml. Neither a local or general reaction was observed in the children when such a method was used.

From the first days of treatment, unrest and apathy gradually disappeared in the patients, sleep and appetite improved, and the children began to gain weight. The general condition became satisfactory and the temperature dropped to normal figures. Normalization of temperature was reached by the 25th day of treatment in 37 children of the 1st group, and by the 56th day in the remaining 10, while in the control group the tempera-

ture became normal during the first month of treatment in 25 children, and in 17 it took 70 days from the onset of treatment.

Pyemic foci were liquidated in various periods. In 42 children of the first group they disappeared during the course of a month from the onset of treatment with staphylococcal toxoid, and in 2 patients - later. In 3 children, repeated waves of newly appearing purulent foci were observed in the second month of treatment. In 2 patients, this was due to an interrupted course of treatment with toxoid.

In the 2nd group the pyemic foci disappeared in 23 children during the 1st month. In the remaining 18, repeated waves were often noted with the appearance of new purulent foci in the course of 2 months, and in only one was recovery not achieved.

The periods for the improvement of the general condition and the disappearance of pyemic foci were reflected in the periods of recovery. In the 1st group 26 children recovered by the 30th day of their stay in the clinic, 18 children by the 50th day, and 3 children were discharged with some improvement. It should be noted that 7 recovered children were kept in the clinic up to 2½-3 months for reasons not connected with the disease. In the 2nd group only 15 children recovered by the 30th day, 22 by the 50th day, and the remaining 5 children - in later periods (on the 88th day). (All of these were discharged in a satisfactory condition, except 4 children, discharged with improvement and one child without improvement.)

Changes in hematological indices also took place diversely. It was established that in the children of the 1st group the tendency for an increase in the number of erythrocytes was somewhat more expressed in comparison with the patients of the control group. No difference could be noticed in the increase in the content of hemoglobin among these groups of patients. An increased number of leukocytes - from 14,000 up to 25,000 - was observed in 17 children of the 1st group. During the process of treatment normalization set in in 3 weeks in 15 of the patients. In the control group, of 23 children with the number of leukocytes ranging from 14,000 to 28,000, normalization set in during the same period in only 6 children. Consequently, in the 1st group the number of leukocytes became normal more rapidly than in the control group.

In a large number of children of the 1st group an accelerated ESR was observed prior to treatment. This was lowered during the process of therapy. In one child it did not change, and in 2 patients it even increased by the end of their stay in the clinic. In the control group the accelerated ESR was also lowered under the influence of treatment, however the degree of lowering was less significant in comparison with the patients who received toxoid. Besides this, in a comparatively large number of patients (7 children), a speeding up of the ESR was noted by the end of the observation.

Consequently, as a result of using toxoid, an earlier and more noticeable lowering of the ESR was observed in the children.

Apart from the clinical observation of the children a bacteriological investigation of the pus and blood was performed. In the 1st group seedings from the pus of 40 children were made. Staphylococci were isolated in 39 cases. This included 34 strains of aureus and 5 strains of albus. During the bacteriological investigation of the blood staphylococci were seeded out in 10 children of the 47 investigated. Staphylococcus aureus was isolated in 3 cases, and S. albus in 7.

In the 2nd (control) group the seedings of pus was carried out on 12 children. Staphylococci were isolated in all cases. This included 10 of aureus and 2 of albus. During the seeding of blood in this group staphylococci were seeded out in 15 children out of 42. In 14 cases Staphylococcus albus was isolated and in one case S. aureus.

Thus, a total of 76 strains of staphylococci were isolated. A study of the sensitivity of these strains to antibiotics was performed by the method of paper diagnostic discs.

The majority of the strains of staphylococcus were resistant to biomycin, penicillin, streptomycin and Levomycetin. A sensitivity to erythromycin, colimycin and oxytetracycline was determined in only some of the strains. These investigations showed that the sensitivity of staphylococci to these antibiotics was more expressed. Thus, all the investigated strains were sensitive to colimycin and the greater majority to erythromycin and oxytetracycline.

For the purpose of studying the immunological response of a child to the administration of staphylococcal toxoid we determined the content of staphylococcal antitoxin in the blood before and after the administration of the preparation. Prior to immunization 46 children were investigated, and after immunization - 33 children. It was established here that prior to the administration of the toxoid the amount of staphylococcal antitoxin fluctuated from 0.125 up to 2 AU. The average titer equaled 0.70 ± 0.078 AU.

Following treatment, the content of antitoxin in the blood increased in all the children and fluctuated within 1-16 AU. In the majority of children the titer was within the limits of 3-4 AU, and only in individual cases between 10-16 AU. The average titer of antitoxin equaled 3.35 ± 0.49 AU.

The content of antitoxin was also determined in the blood of 10 children in the control group after the treatment. In them the antibody level fluctuated within the limits of 0.25-2 AU and the average titer of antitoxin equaled 0.77 ± 0.16 AU. Consequently, the clinical recovery of children in the control group was not accompanied by an increase in the titers of antitoxin. Therefore,

the antibody titers in the children treated with the toxoid testifies to an increase in the specific immunological reactivity of the organism under the influence of toxoid.

Since we used the staphylococcal toxoid in various doses, the amount of antitoxin in the blood was analyzed separately depending on the amount of the preparation administered (Table 3).

It can be seen from the data in Table 3 that following the administration of various doses of staphylococcal toxoid we observed a statistically reliable increase in the level of antitoxin in the blood in the children. The use of larger doses of toxoid led to a more considerable accumulation of antitoxin.

Conclusions

1. The use of staphylococcal toxoid in conjunction with other medicines exerted a favorable influence on the course and outcome of staphylococcal diseases in babies.

2. The administration of toxoid furthered a reduction in the period for recovery, a more rapid disappearance of pyemic foci and an earlier normalization of hematological indices.

3. The use of staphylococcal toxoid led to an increase in the specific immunological reactivity of the child. This was indicated by an increase in the titers of staphylococcal antitoxin in the blood.

4. Following the administration of native staphylococcal toxoid a noticeable local and general reaction was not observed.

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Table 1

Clinical characteristics of the sick children

Group of children	Number of children	Age				Rearing			Hypotropia			Rickets	
		from 8 days to 1 month	$1\frac{1}{2}$ - 3 months	$3\frac{1}{2}$ - 6 months	7--12 months	Breast	Mixed	Artificial	I level	II level	III level	Stage I	Stage II
Received staphylococcal toxoid (1st group)	47	8	22	11	6	14	15	18	15	18	-	11	19
Control (2nd group)	42	5	19	16	2	6	17	19	15	18	3	11	19
Total	89	13	41	27	8	20	32	37	30	36	3	22	38

Table 2

Clinical manifestations and the severity of the course of illness

Group of patients	Number of children	Diagnosis			Course	
		Septico-pyemia	Pyoderma	Otitis	Severe	Moderate severity
Received staphylococcal toxoid (1st group)	47	25	17	5	23	24
Control (2nd group)	42	30	12	-	19	23
Total	89	55	29	5	42	47

Table 3

Average titers of antitoxin in children who had received different doses of toxoid

Dosage of toxoid	Average titer of antitoxin (in AU)				Coefficient of reliability, t	% reliability
	prior to immunization		after immunization			
	Number investigated, n	$M \pm m$	Number investigated, n	$M_1 \pm m_1$		
Large doses	20	0.86 ± 0.123	20	4.07 ± 0.83	3.80	more than 99
Small doses	26	0.57 ± 0.036	13	2.3 ± 0.3	5.28	more than 99